```
=> e fensterle joachim/au
E1            4     FENSTERL VOLKER/AU
E2           14     FENSTERLE J/AU
E3           41 --> FENSTERLE JOACHIM/AU
E4            1     FENSTERLE ROLF/AU
E5            1     FENSTERMACH MARC J/AU
E6            2     FENSTERMACHER C/AU
E7           17     FENSTERMACHER C A/AU
E8            3     FENSTERMACHER CHARLES/AU
E9            1     FENSTERMACHER CHARLES A/AU
E10           3     FENSTERMACHER D/AU
E11          13     FENSTERMACHER D A/AU
E12           1     FENSTERMACHER D J/AU

=> s e2-e3
L1           55 ("FENSTERLE J"/AU OR "FENSTERLE JOACHIM"/AU)

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2            23 DUP REM L1 (32 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 23 ANSWERS - CONTINUE? Y/(N):y

L2   ANSWER 1 OF 23  CAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
AN   2007:413545  CAPLUS
DN   146:427951
TI   Vivotif - A 'Magic Shield' for Protection against Typhoid Fever and
     Delivery of Heterologous Antigens
AU   Gentschev, Ivaylo; Spreng, Simone; Sieber, Heike; Ures, Jose; Mollet,
     Fabian; Collioud, Andre; Pearman, Jon; Griot-Wenk, Monika E.;
     Fensterle, Joachim; Rapp, Ulf R.; Goebel, Werner; Rothen, Simon
     A.; Dietrich, Guido
CS   Institut fur Medizinische Strahlenkunde und Zellforschung (MSZ),
     University of Wurzburg, Wurzburg, Germany
SO   Chemotherapy (Basel, Switzerland) (2007), 53(3), 177-180
     CODEN: CHTHBK; ISSN: 0009-3157
PB   S. Karger AG
DT   Journal; General Review
LA   English
AB   A review.  The attenuated Salmonella typhi strain Ty21a is the main
     constituent of Vivotif, the only attenuated live oral vaccine against
     typhoid fever.  In comparison with antibiotics, the magic bullets' which
     Paul Ehrlich was striving for to treat infectious diseases, this vaccine
     should be viewed as a 'magic shield', because rather than treating typhoid
     fever after the infection has started, immunization with this vaccine
     strain prevents infection and disease by the induction of specific immune
     responses.  Ty21a is also an attractive carrier for the delivery of
     heterologous antigens.  Recently, we successfully used Ty21a for antigen
     delivery via the haemolysin secretion system of Escherichia coli, which
     allows efficient protein secretion from the carrier bacteria.

L2   ANSWER 2 OF 23     MEDLINE on STN
AN   2006220410     MEDLINE
DN   PubMed ID: 16626317
TI   [A trip through the signaling pathways of melanoma].
     Ein Streifzug durch die (Signal-)Wege des malignen Melanoms.
AU   Fensterle Joachim
CS   Universitat Wurzburg, Institut fur Med. Strahlenkunde und Zellforschung
     (MSZ), Wurzburg.. joachim.fensterle@mail.uni-wuerzburg.de
SO   Journal der Deutschen Dermatologischen Gesellschaft = Journal of the
     German Society of Dermatology : JDDG, (2006 Mar) Vol. 4, No. 3, pp.
     205-17.  Ref: 83
```

Journal code: 101164708. ISSN: 1610-0379.
CY Germany: Germany, Federal Republic of
DT (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA German
FS Priority Journals
EM 200605
ED Entered STN: 22 Apr 2006
Last Updated on STN: 26 May 2006
Entered Medline: 25 May 2006
AB Many cellular signaling pathways are involved in the development of cancer. Depending on the tumor entity, the nature as well as the mode of activation can differ. Some signaling pathways frequently show changes as all tumor cells have to fulfill some basic requirements such as independence from growth factors or insensitivity against apoptosis. In this review, the possibilities of a tumor to manipulate signaling pathways to reach these goals are exemplified based on an archetypical melanoma cell. In addition, new therapeutic options based on the knowledge of signaling pathways will be discussed.

L2 ANSWER 3 OF 23 MEDLINE on STN
AN 2006182516 MEDLINE
DN PubMed ID: 16533402
TI HLA-B8 association with late-stage melanoma--an immunological lesson?.
AU Fensterle Joachim; Trefzer Uwe; Berger Thomas; Andersen Mads Hald; Ugurel Selma; Becker Jurgen C
CS Inst. f. Med. Strahlenkunde und Zellforschung MSZ, University Clinics of Wurzburg, Versbacher Str. 5, 97078 Wurzburg, Germany.. joachim.fensterle@mail.uni-wuerzburg.de
SO BMC medicine, (2006) Vol. 4, pp. 5. Electronic Publication: 2006-03-13.
Journal code: 101190723. E-ISSN: 1741-7015.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200604
ED Entered STN: 4 Apr 2006
Last Updated on STN: 19 Apr 2006
Entered Medline: 18 Apr 2006
AB BACKGROUND: Differences in HLA allele frequencies between the diseased and healthy populations may signify efficient immune responses, a notion that has been successfully tested for infectious diseases or for association with genetic elements involved in a distinct type of immunity. This retrospective study is intended to detect differences in MHC class I carrier frequencies of advanced melanoma patients compared to healthy bone marrow donors. METHODS: The HLA-A and -B carrier frequencies of 748 stage IV melanoma patients retrieved from serotyping at 6 different centers in Germany were compared using a chi-square test to 13,386 fully HLA typed bone marrow donors registered in the German national bone marrow donor registry. RESULTS: The comparison of HLA carrier frequencies in advanced cancer patients with healthy bone marrow donors revealed a significant decrease in HLA-B8 carrier frequencies, which was also apparent in patients with advanced disease compared to patients with loco-regional disease. CONCLUSION: The data suggest that protective immune responses restricted to distinct MHC class I molecules may be operational in a subset of melanoma patients, which is the prerequisite for a large scale screen for the corresponding epitopes. Alternatively, the known association of the ancestral haplotype HLA-A1, -B8 and -DR3 with genetic elements such as distinct TNF-alpha alleles might have a protective effect on disease progression. In any case, identification of the cause of protection within this patient subset might lead to a significant improvement in the efficacy of current immunotherapeutic approaches.

L2 ANSWER 4 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2
AN 2007:276509 BIOSIS
DN PREV200700260599
TI HLA-B8 association with late-stage melanoma - an immunological lesson?.
AU Fensterle, Joachim [Reprint Author]; Trefzer, Uwe; Berger, Thomas; Andersen, Mads Hald; Ugurel, Selma; Becker, Juergen C.
CS Univ Clin Wurzburg, Inst Med Strahlenkunde and Zellforsch MSZ, Versbacher Str 5, D-97078 Wurzburg, Germany
joachim.fensterle@mail.uni-wuerzburg.de; uwe.trefzer@charite.de; Thomas.Berger@derma.imed.uni-erlangen.de; mha@cancer.dk; selma.ugurel@gmx.de; becker_jc@klinik.uni-wuerzburg.de
SO BMC Medicine, (MAR 13 2006) Vol. 4.
ISSN: 1741-7015. E-ISSN: 1741-7015.
DT Article
LA English
ED Entered STN: 25 Apr 2007
Last Updated on STN: 25 Apr 2007
AB Background: Differences in HLA allele frequencies between the diseased and healthy populations may signify efficient immune responses, a notion that has been successfully tested for infectious diseases or for association with genetic elements involved in a distinct type of immunity. This retrospective study is intended to detect differences in MHC class I carrier frequencies of advanced melanoma patients compared to healthy bone marrow donors.Methods: The HLA-A and -B carrier frequencies of 748 stage IV melanoma patients retrieved from serotyping at 6 different centers in Germany were compared using a chi-square test to 13,386 fully HLA typed bone marrow donors registered in the German national bone marrow donor registry.Results: The comparison of HLA carrier frequencies in advanced cancer patients with healthy bone marrow donors revealed a significant decrease in HLA-B8 carrier frequencies, which was also apparent in patients with advanced disease compared to patients with loco-regional disease.Conclusion: The data suggest that protective immune responses restricted to distinct MHC class I molecules may be operational in a subset of melanoma patients, which is the prerequisite for a large scale screen for the corresponding epitopes. Alternatively, the known association of the ancestral haplotype HLA-A1, -B8 and -DR3 with genetic elements such as distinct TNF-alpha alleles might have a protective effect on disease progression. In any case, identification of the cause of protection within this patient subset might lead to a significant improvement in the efficacy of current immunotherapeutic approaches.

L2 ANSWER 5 OF 23 MEDLINE on STN
AN 2005090722 MEDLINE
DN PubMed ID: 15703070
TI Use of a recombinant Salmonella enterica serovar Typhimurium strain expressing C-Raf for protection against C-Raf induced lung adenoma in mice.
AU Gentschev Ivaylo; Fensterle Joachim; Schmidt Andreas; Potapenko Tamara; Troppmair Jakob; Goebel Werner; Rapp Ulf R
CS Institut fur Medizinische Strahlenkunde und Zellforschung (MSZ), University of Wuerzburg, D-97078 Wuerzburg, Germany..
ivaylo.gentschev@mail.uni-wuerzburg.de
SO BMC cancer, (2005 Feb 9) Vol. 5, pp. 15. Electronic Publication: 2005-02-09.
Journal code: 100967800. E-ISSN: 1471-2407.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200510
ED Entered STN: 23 Feb 2005
Last Updated on STN: 18 Oct 2005

Entered Medline: 17 Oct 2005

AB BACKGROUND: Serine-threonine kinases of the Raf family (A-Raf, B-Raf, C-Raf) are central players in cellular signal transduction, and thus often causally involved in the development of cancer when mutated or over-expressed. Therefore these proteins are potential targets for immunotherapy and a possible basis for vaccine development against tumors. In this study we analyzed the functionality of a new live C-Raf vaccine based on an attenuated Salmonella enterica serovar Typhimurium aroA strain in two Raf dependent lung tumor mouse models. METHODS: The antigen C-Raf has been fused to the C-terminal secretion signal of Escherichia coli alpha-hemolysin and expressed in secreted form by an attenuated aroA Salmonella enterica serovar Typhimurium strain via the alpha-hemolysin secretion pathway. The effect of the immunization with this recombinant C-Raf strain on wild-type C57BL/6 or lung tumor bearing transgenic BxB mice was analyzed using western blot and FACS analysis as well as specific tumor growth assays. RESULTS: C-Raf antigen was successfully expressed in secreted form by an attenuated Salmonella enterica serovar Typhimurium aroA strain using the E. coli hemolysin secretion system. Immunization of wild-type C57BL/6 or tumor bearing mice provoked specific C-Raf antibody and T-cell responses. Most importantly, the vaccine strain significantly reduced tumor growth in two transgenic mouse models of Raf oncogene-induced lung adenomas. CONCLUSIONS: The combination of the C-Raf antigen, hemolysin secretion system and Salmonella enterica serovar Typhimurium could form the basis for a new generation of live bacterial vaccines for the treatment of Raf dependent human malignancies.

L2 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

AN 2005:240459 CAPLUS

DN 142:390617

TI Use of a recombinant Salmonella enterica serovar Typhimurium strain expressing C-Raf for protection against C-Raf induced lung adenoma in mice

AU Gentschev, Ivaylo; Fensterle, Joachim; Schmidt, Andreas; Potapenko, Tamara; Troppmair, Jakob; Goebel, Werner; Rapp, Ulf R.

CS Institut fuer Medizinische Strahlenkunde und Zellforschung (MSZ), University of Wuerzburg, Wuerzburg, D-97078, Germany

SO BMC Cancer (2005), 5, No pp. given
CODEN: BCMACL; ISSN: 1471-2407
URL: http://www.biomedcentral.com/content/pdf/1471-2407-5-15.pdf

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Serine-threonine kinases of the Rat family (A-Raf, B-Raf, C-Raf) are central players in cellular signal transduction, and thus often causally involved in the development of cancer when mutated or over-expressed. Therefore, these proteins are potential targets for immunotherapy and a possible basis for vaccine development against tumors. In this study we analyzed the functionality of a new live C-Raf vaccine based on an attenuated Salmonella enterica serovar Typhimurium AroA strain in two Raf dependent lung tumor mouse models. The antigen C-Raf has been fused to the C-terminal secretion signal of Escherichia coli α-hemolysin and expressed in secreted form by an attenuated aroA Salmonella enterica serovar Typhimurium strain via the α-hemolysin secretion pathway. The effect of the immunization with this recombinant C-Raf strain on wild-type C57BL/6 or lung tumor bearing transgenic BxB mice was analyzed using western blot and FACS anal. as well as specific tumor growth assays. C-Raf antigen was successfully expressed in secreted form by an attenuated Salmonella enterica serovar Typhimurium aroA strain using the E. coli hemolysin secretion system. Immunization of wild-type C57BL/6 or tumor bearing mice provoked specific C-Raf antibody and T-cell responses. Most importantly, the vaccine strain significantly reduced tumor growth in two transgenic mouse models of Raf oncogene-induced lung adenomas. The combination of the C-Raf antigen, hemolysin secretion system and Salmonella enterica serovar Typhimurium could form the basis for a new generation of live bacterial vaccines for the treatment of Raf dependent

human malignancies.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1080811 CAPLUS
DN 142:22299
TI Cells used as carriers for bacteria in the therapy of cancer and other diseases
IN Fensterle, Joachim; Goebel, Werner; Rapp, Ulf; Strizker, Jochen; Schmidt, Andreas; Gentschev, Ivaylo; Potapenko, Tamara
PA Medinnova Gesellschaft fuer Innovationen aus Akademischer Forschung m.b.H., Germany
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2004108155 | A1 | 20041216 | WO 2004-DE1178 | 20040607 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10326187 | A1 | 20050105 | DE 2003-10326187 | 20030606 |
| AU 2004244701 | A1 | 20041216 | AU 2004-244701 | 20040607 |
| CA 2526789 | A1 | 20041216 | CA 2004-2526789 | 20040607 |
| EP 1631310 | A1 | 20060308 | EP 2004-738631 | 20040607 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| CN 1802175 | A | 20060712 | CN 2004-80015761 | 20040607 |
| BR 2004011210 | A | 20060718 | BR 2004-11210 | 20040607 |
| JP 2006526396 | T | 20061124 | JP 2006-508123 | 20040607 |
| IN 2005MN01351 | A | 20060519 | IN 2005-MN1351 | 20051202 |
| NO 2006000095 | A | 20060303 | NO 2006-95 | 20060106 |
| US 2006240038 | A1 | 20061026 | US 2006-559663 | 20060621 |
| PRAI DE 2003-10326187 | A | 20030606 | | |
| WO 2004-DE1178 | W | 20040607 | | |

AB The invention relates to the use of a cell, which is charged with a microorganism that contains foreign DNA, in particular a bacterial microorganism, to produce a pharmaceutical composition Preferably, the foreign DNA codes for a defined active agent and the pharmaceutical composition is designed for use in the prophylaxis or treatment of a disease that can be treated with said active agent.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 4
AN 2004:396556 BIOSIS
DN PREV200400395364
TI Immunogenicity of constitutively active V599EBRaf.
AU Andersen, Mads Hald; Fensterle, Joachim; Ugurel, Selma; Reker, Sine; Houben, Roland; Guldberg, Per; Berger, Thomas G.; Schadendorf, Dirk; Trefzer, Uwe; Broecker, Eva-B.; Straten, Per thor; Rapp, Ulf R.; Becker, Juergen C. [Reprint Author]

CS Dept Dermatol and Dermatooncol, Univ Wurzburg, Josef Schneider Str 2, D-97078, Wurzburg, Germany
becker_jc@klinik.uni-wuerzburg.de
SO Cancer Research, (August 1 2004) Vol. 64, No. 15, pp. 5456-5460. print.
ISSN: 0008-5472 (ISSN print).
DT Article
LA English
ED Entered STN: 13 Oct 2004
Last Updated on STN: 13 Oct 2004
AB Activating BRAF somatic missense mutations within the kinase domain are present in 60-66% of melanomas. The vast majority of these represent a single substitution of glutamate for valine (V599E). Here, we demonstrate spontaneous HLA-B*2705-restrieted cytotoxic T-cell responses against an epitope derived from V599EBRaf. These T-cell responses were mutation specific as the corresponding epitope derived from wildtype BRaf was not recognized. The loss of the V599EBRAF genotype during progression from primary to metastatic melanoma in patients with V599EBRaf specific T-cell responses suggests an active immune selection of nonmutated melanoma clones by the tumor-bearing host.

L2 ANSWER 9 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 5
AN 2004:383924 BIOSIS
DN PREV200400382268
TI Enhanced protective efficacy of a tuberculosis DNA vaccine by adsorption onto cationic PLG microparticles.
AU Mollenkopf, Hans-Joachim [Reprint Author]; Dietrich, Guido; Fensterle, Joachim; Grode, Leander; Diehl, Klaus-Dieter; Knapp, Bernhard; Singh, Manmohan; O'Hagan, Derek T.; Ulmer, Jeffrey B.; Kaufmann, Stefan H. E.
CS Dept ImmunolMPI Infect Biol, Max Planck Inst Infect Biol, Schumannstr 21-22, D-10117, Berlin, Germany
mollenkopf@mpiib-berlin.mpg.de
SO Vaccine, (July 29 2004) Vol. 22, No. 21-22, pp. 2690-2695. print.
ISSN: 0264-410X (ISSN print).
DT Article
LA English
ED Entered STN: 29 Sep 2004
Last Updated on STN: 29 Sep 2004
AB Immunization with plasmid DNA vectors represents a promising new approach to vaccination. It has been shown to elicit humoral and cellular immunity and protection in various infection models. Here, we assessed the immunogenicity and protective efficacy of a DNA vaccine vector encoding the antigen 85A (Ag85A) of Mycobacterium tuberculosis. Since intramuscular (i.m.) immunization with naked DNA requires considerable amounts of DNA in order to be effective, we evaluated a strategy to reduce the amount of DNA needed. To this end, we used Ag85A DNA adsorbed onto cationic poly(DL-lactide-co-glycolide) (PLG) microparticles and observed similar levels of protection against aerosol challenge in mice using doses of PLG-DNA two orders of magnitude lower than with naked DNA itself.


L2 ANSWER 10 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
AN 2005:96289 BIOSIS
DN PREV200500096512
TI Use of the alpha-hemolysin secretion system of Escherichia coli for antigen delivery in the Salmonella typhi Ty21a vaccine strain.
AU Gentschev, Ivaylo [Reprint Author]; Dietrich, Guido; Spreng, Simone; Neuhaus, Beatrice; Maier, Elke; Benz, Roland; Goebel, Werner; Fensterle, Joachim; Rapp, Ulf R.
CS Inst Med Strahlenkunde and ZellforschMSZ, Univ Wurzburg, Verbacher Str 5, D-97078, Wurzburg, Germany
ivaylo.gentschev@mait.uni-wuerzburg.de

SO IJMM International Journal of Medical Microbiology, (October 2004) Vol. 294, No. 6, pp. 363-371. print.
ISSN: 1438-4221 (ISSN print).
DT Article
LA English
ED Entered STN: 9 Mar 2005
Last Updated on STN: 9 Mar 2005
AB This study examined the suitability of the hemolysin secretion system of Escherichia coli for expression and delivery of alpha-hemolysin (HlyA) by the S. typhi Ty21a strain, the only live oral Salmonella vaccine strain licensed for human use, under in vitro and in vivo conditions. For this purpose, two plasmid vectors encoding either the whole a-hemolysin of E. coli (pANN202-812/pMOhly2) or the hemolysin secretion signal (pMOhly1) were transferred into S. typhi Ty21a. S. typhi Ty21a carrying pANN202-812/pMOhly2 revealed efficient secretion of hemolysin in vitro. After formulation according to a process suitable for commercial production of Salmonella-based live bacterial vaccines, plasmids were shown to be stable in Ty21a and hemolysin secretion was demonstrated even after storage of the strains under real-time and stress conditions. After intranasal immunization of mice with S. typhi Ty21a/pANN202-812 plasmids are stable in vivo, and immunization induced a profound immune response against the heterologous HlyA antigen. Therefore, the combination of the hemolysin secretion system and S. typhi Ty21a could form the basis for a new generation of live bacterial vaccines. 

L2 ANSWER 11 OF 23 MEDLINE on STN
AN 2004478998 MEDLINE
DN PubMed ID: 15361259
TI B-Raf specific antibody responses in melanoma patients.
AU Fensterle Joachim; Becker Jurgen C; Potapenko Tamara; Heimbach Veronika; Vetter Claudia S; Brocker Eva B; Rapp Ulf R
CS Institut fur Medizinische Strahlenkunde und Zellforschung (MSZ), University Clinics of Wurzburg, Versbacher Str. 5, 97078 Wurzburg, Germany.. joachim.fensterle@mail.uni-wuerzburg.de
SO BMC cancer, (2004 Sep 12) Vol. 4, pp. 62. Electronic Publication: 2004-09-12.
Journal code: 100967800. E-ISSN: 1471-2407.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200503
ED Entered STN: 28 Sep 2004
Last Updated on STN: 9 Mar 2005
Entered Medline: 8 Mar 2005
AB BACKGROUND: Mutations of the BRAF gene are the most common genetic alteration in melanoma. Moreover, BRAF mutations are already present in benign nevi. Being overexpressed and mutated, B-Raf is a potential target for the immune system and as this mutation seems to be an early event, a humoral immune response against this antigen might serve as a diagnostic tool for detection of high risk patients. METHODS: 372 sera of 148 stage IV melanoma patients and 119 sera of non-melanoma patients were screened for B-Raf, B-Raf V599E and C-Raf specific antibodies by an ELISA assay. Sera were screened for specific total Ig and for IgG. Serum titers were compared with a two tailed Mann-Whitney U test. Sera with titers of 1:300 or higher were termed positive and groups were compared with a two tailed Fisher's exact test. RESULTS: B-Raf specific antibodies recognizing both B-Raf and B-Raf V599E were detected in 8.9% of the sera of melanoma patients and in 2,5% of the control group. Raf specific IgG was detected in some patients at very low levels. B-Raf specific antibody responses did not correlate with clinical parameters but in some cases, B-Raf antibodies emerged during disease progression. CONCLUSION: These findings

imply that B-Raf is immunogenic in melanoma patients and that it might serve as a potential target for immunotherapy. However, B-Raf specific antibodies emerge at rather late stages of melanoma progression and are present only with a low frequency indicating that spontaneous B-Raf specific antibodies are not an early marker for melanoma, but rather may serve as a therapeutic target.

L2 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 7
AN 2004:832664 CAPLUS
DN 141:311824
TI B-Raf specific antibody responses in melanoma patients
AU Fensterle, Joachim; Becker, Jurgen C.; Potapenko, Tamara; Heimbach, Veronika; Vetter, Claudia S.; Brocker, Eva B.; Rapp, Ulf R.
CS Institut fuer Medizinische Strahlenkunde und Zellforschung (MSZ), University Clinics of Wuerzburg, Wuerzburg, 97078, Germany
SO BMC Cancer (2004), 4, No pp. given
CODEN: BCMACL; ISSN: 1471-2407
URL: http://www.biomedcentral.com/content/pdf/1471-2407-4-62.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Background Mutations of the BRAF gene are the most common genetic alteration in melanoma. Moreover, BRAF mutations are already present in benign nevi. Being overexpressed and mutated, B-Raf is a potential target for the immune system and as this mutation seems to be an early event, a humoral immune response against this antigen might serve as a diagnostic tool for detection of high risk patients. Methods 372 sera of 148 stage IV melanoma patients and 119 sera of non-melanoma patients were screened for B-Raf, B-Raf V599E and C-Raf specific antibodies by an ELISA assay. Sera were screened for specific total Ig and for IgG. Serum titers were compared with a two tailed Mann-Whitney U test. Sera with titers of 1:300 or higher were termed pos. and groups were compared with a two tailed Fisher's exact test. Results: B-Raf specific antibodies recognizing both B-Raf and B-Raf V599E were detected in 8.9 % of the sera of melanoma patients and in 2.5 % of the control group. Raf specific IgG was detected in some patients at very low levels. B-Raf specific antibody responses did not correlate with clin. parameters but in some cases, B-Raf antibodies emerged during disease progression. Conclusion: These findings imply that B-Raf is immunogenic in melanoma patients and that it might serve as a potential target for immunotherapy. However, B-Raf specific antibodies emerge at rather late stages of melanoma progression and are present only with a low frequency indicating that spontaneous B-Raf specific antibodies are not an early marker for melanoma, but rather may serve as a therapeutic target.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:697071 CAPLUS
DN 139:224411
TI Transgenic microorganisms producing cell antigens for use as vaccines, especially tumor vaccines
IN Rapp, Ulf R.; Goebel, Werner; Gentschev, Ivaylo; Fensterle, Joachim
PA Medinnova Gesellschaft fuer Medizinische Innovationen aus Akademischer Forschung m.b.H., Germany
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003072789 | A2 | 20030904 | WO 2003-DE471 | 20030213 |

WO 2003072789 A3 20040212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10208653 A1 20030918 DE 2002-10208653 20020228
CA 2513190 A1 20030904 CA 2003-2513190 20030213
AU 2003206664 A1 20030909 AU 2003-206664 20030213
EP 1478756 A2 20041124 EP 2003-704315 20030213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005518795 T 20050630 JP 2003-571470 20030213
CN 1650014 A 20050803 CN 2003-809598 20030213
NO 2004003926 A 20040920 NO 2004-3926 20040920
IN 2004KN01389 A 20060526 IN 2004-KN1389 20040920
US 2006105423 A1 20060518 US 2005-506096 20050611
PRAI DE 2002-10208653 A 20020228
WO 2003-DE471 W 20030213

AB The invention relates to a microorganism expressing a chimeric gene encoding a cell antigen. The chimeric gene comprises (1) a sequence coding for at least one epitope of a tumor antigen and/or of an antigen specific for the tissue from which the tumor originates; (2) an optional sequence coding for a protein that stimulates cells of the immune system; (3a) a sequence coding for a transport system which makes it possible to secrete or display on the microbial surface the chimeric gene product; and/or (3b) a sequence encoding a protein used for lysing the microorganisms in the cytosol of mammalian cells and for intracellularly releasing plasmids which are contained in the lysed microorganisms; and (4) a promoter for expressing the chimeric gene which is capable of being activated in the microorganism, is tissue--specific but not cell-specific. Also disclosed is the use of such microorganisms as tumor vaccines. Thus, c-raf-expressing transgenic mice were orally immunized with attenuated Salmonella typhimurium containing plasmid pMO-Raf. This plasmid contains a chimeric gene consisting of human c-Raf cDNA fused to hlyA. This immunization overcame the self-tolerance of C-Raf and led to a CD4+ T cell response. The lung tumor mass in these mice was less than that in control mice.

L2 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:656908 CAPLUS
DN 139:202434
TI Bacteria protected from phagocytosis by plasma proteins for the targeted delivery of therapeutic genes and proteins to specific cell types
IN Goebel, Werner; Rapp, R. Ulf; Sedlacek, Hans-Harald; Fensterle, Joachim; Gentschev, Ivaylo
PA Medinnova Gesellschaft fuer Medizinische Innovationen aus Akademischer Forschung m.b.H., Germany
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003068954 | A2 | 20030821 | WO 2003-DE470 | 20030213 |
| | WO 2003068954 | A3 | 20031016 | | |
| | WO 2003068954 | A8 | 20051013 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| DE | 10206325 | A1 | 20030904 | DE 2002-10206325 | 20020214 |
| CA | 2513198 | A1 | 20030821 | CA 2003-2513198 | 20030213 |
| AU | 2003206663 | A1 | 20030904 | AU 2003-206663 | 20030213 |
| EP | 1474519 | A2 | 20041110 | EP 2003-704314 | 20030213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP | 2005517405 | T | 20050616 | JP 2003-568069 | 20030213 |
| CN | 1646693 | A | 20050727 | CN 2003-808244 | 20030213 |
| NO | 2004003800 | A | 20041108 | NO 2004-3800 | 20040910 |
| IN | 2004KN01349 | A | 20060505 | IN 2004-KN1349 | 20040913 |
| ZA | 2004007358 | A | 20051118 | ZA 2004-7358 | 20040914 |
| US | 2005244374 | A1 | 20051103 | US 2005-504944 | 20050523 |
| PRAI DE | 2002-10206325 | A | 20020214 | | |
| WO | 2003-DE470 | W | 20030213 | | |

AB The use of bacteria for the intracellular delivery of cytotoxic or other therapeutic proteins is described. The bacteria use a number of genes for targeting and delivery, including: one or more genes for antiproliferative or cytotoxic products; a constitutively expressed gene for a blood plasma protein, and optionally a gene for a cell-specific ligand. The plasma protein, which may be a fusion protein with a host cell surface protein, is presented on the cell surface to prevent it being phagocytosed before it reaches the target cell for the ligand. The proteins are transferred to the cell surface using a protein transport system for a secreted protein such as a hemolysin. The secretion system may be constitutive or regulated. The bacterium may be turned into a suicide host by introduction of genes for a system that causes the cell to lyse in the cytoplasm of a host cell to release such as cytotoxins retained within the cell or a plasmid carrying an expression cassette for an antigen. The individual components may parts of the same regulatory system or may be under control of independent regulatory systems as needed. The development of strains of Salmonella typhimurium that use the hemolysin secretory pathway to simultaneously present human serum albumin and proteins including human β-glucuronidase or Fas ligand on the cell surface is demonstrated.

L2 ANSWER 15 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:398933 BIOSIS
DN PREV200300398933
TI Raf kinases in lung tumor development.
AU Rapp, Ulf R. [Reprint Author]; Fensterle, Joachim; Albert, Stefan; Goetz, Rudolf
CS Institut fuer Medizinische, Strahlenkunde und Zellforschung (MSZ), Bayerische Julius-Maximilians-Universitaet, Universitaet Wuerzburg, Versbacher-Strasse 5, D-97078, Wuerzburg, Germany
rappur@mail.uni-wuerzburg.de
SO Weber, George [Editor, Reprint Author]. Adv. Enzyme Regul., (2003) pp. 183-195. Advances in Enzyme Regulation. Volume 43. print.
Publisher: Elsevier Science Ltd., The Boulevard, Langford Lane, Kidlington, Oxon, OX5 1GB, UK; Elsevier Science Inc., 660 White Plains Road, Tarrytown, NY, 10591-5153, USA. Series: Advances in Enzyme Regulation.
Meeting Info.: Forty-Third International Symposium on Regulation of Enzyme Activity and Synthesis in Normal and Neoplastic Tissues. Indianapolis, IN, USA. September 23-24, 2002.

CODEN: AEZRA2. ISSN: 0065-2571. ISBN: 0-080-44294-3 (cloth).
DT Book; (Book Chapter)
Conference; (Meeting)
Conference; (Meeting Paper)
LA English
ED Entered STN: 27 Aug 2003
Last Updated on STN: 27 Aug 2003

L2 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 8
AN 2003:923217 CAPLUS
DN 140:336584
TI Raf kinases in lung tumor development
AU Rapp, Ulf R.; Fensterle, Joachim; Albert, Stefan; Goetz, Rudolf
CS Institut fuer Medizinische, Strahlenkunde und Zellforschung, Bayerische Julius-Maximilians-Universitaet Wuerzburg, Wuerzburg, D-97078, Germany
SO Advances in Enzyme Regulation (2003), 43, 183-195
CODEN: AEZRA2; ISSN: 0065-2571
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
AB A review on the role of Raf kinases in lung tumor development and as targets for bacterial immunotherapy. It has been shown that live heterologous bacterial vaccines carrying Raf antigens might be a promising approach for further Raf-based immunotherapies.
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 9
AN 2003:7469 BIOSIS
DN PREV200300007469
TI Cell-mediated immunity induced by recombinant Mycobacterium bovis Bacille Calmette-Guerin strains against an intracellular bacterial pathogen: Importance of antigen secretion or membrane-targeted antigen display as lipoprotein for vaccine efficacy.
AU Grode, Leander; Kursar, Mischo; Fensterle, Joachim; Kaufmann, Stefan H. E. [Reprint Author]; Hess, Juergen
CS Department of Immunology, Max-Planck-Institute for Infection Biology, D-10117, Berlin, Germany
kaufmann@mpiib-berlin.mpg.de
SO Journal of Immunology, (February 15 2002) Vol. 168, No. 4, pp. 1869-1876. print.
ISSN: 0022-1767 (ISSN print).
DT Article
LA English
ED Entered STN: 18 Dec 2002
Last Updated on STN: 18 Dec 2002
AB Live recombinant vaccines expressing defined pathogen-derived Ags represent powerful candidates for future vaccination strategies. In this study, we report on the differential induction of protective cell-mediated immunity elicited by different recombinant Mycobacterium bovis Bacille Calmette-Guerin (BCG) strains displaying p60 Ag of Listeria monocytogenes in secreted, cytosolic, or membrane-attached form for T cell recognition. Anti-listerial protection evoked by the membrane-linked p60 lipoprotein of rBCG Mp60 and that of the p60 derivative secreted by rBCG Sp60-40 were nearly equal, whereas cytosolic p60 displayed by rBCG Np60 failed to protect mice from listeriosis. In vivo depletion of CD4 or CD8 T cell subpopulations in rBCG Mp60-vaccinated mice before listerial challenge revealed interactions of both T cell subsets in anti-listerial protection. In rBCG Sp60-40-vaccinated animals, CD4 T cells predominantly contributed to anti-listerial control as shown by the failure of anti-CD8 mAb treatment to impair the outcome of listeriosis in rBCG Sp60-40-vaccinated mice after L. monocytogenes challenge. Hence, differential Ag display by rBCG influences cell-mediated immunity, which in turn may impact vaccine

efficacy due to the different requirements of CD4 or CD8 T cells for pathogen elimination.

L2 ANSWER 18 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 10
AN 2003:39570 BIOSIS
DN PREV200300039570
TI Regulatory CD4+CD25+ T cells restrict memory CD8+ T cell responses.
AU Kursar, Mischo; Bonhagen, Kerstin; Fensterle, Joachim; Koehler, Anne; Hurwitz, Robert; Kamradt, Thomas; Kaufmann, Stefan H. E.; Mittruecker, Hans-Willi [Reprint Author]
CS Max Planck Institute for Infection Biology, Schumannstr. 21/22, 10117, Berlin, Germany
mittruecker@mpiib-berlin.mpg.de
SO Journal of Experimental Medicine, (December 16 2002) Vol. 196, No. 12, pp. 1585-1592. print.
ISSN: 0022-1007 (ISSN print).
DT Article
LA English
ED Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003
AB CD4+ T cell help is important for the generation of CD8+ T cell responses. We used depleting anti-CD4 mAb to analyze the role of CD4+ T cells for memory CD8+ T cell responses after secondary infection of mice with the intracellular bacterium Listeria monocytogenes, or after boost immunization by specific peptide or DNA vaccination. Surprisingly, anti-CD4 mAb treatment during secondary CD8+ T cell responses markedly enlarged the population size of antigen-specific CD8+ T cells. After boost immunization with peptide or DNA, this effect was particularly profound, and antigen-specific CD8+ T cell populations were enlarged at least 10-fold. In terms of cytokine production and cytotoxicity, the enlarged CD8+ T cell population consisted of functional effector T cells. In depletion and transfer experiments, the suppressive function could be ascribed to CD4+CD25+ T cells. Our results demonstrate that CD4+ T cells control the CD8+ T cell response in two directions. Initially, they promote the generation of a CD8+ T cell responses and later they restrain the strength of the CD8+ T cell memory response. Down-modulation of CD8+ T cell responses during infection could prevent harmful consequences after eradication of the pathogen.

L2 ANSWER 19 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 11
AN 2001:136457 BIOSIS
DN PREV200100136457
TI Secretion of different listeriolysin cognates by recombinant attenuated Salmonella typhimurium: Superior efficacy of haemolytic over non-haemolytic constructs after oral vaccination.
AU Hess, Juergen [Reprint author]; Grode, Leander; Gentschev, Ivo; Fensterle, Joachim; Dietrich, Guido; Goebel, Werner; Kaufmann, Stefan H. E.
CS november AG, Ulrich-Schalk-Str. 3, D-91056, Erlangen, Germany
hess@november.de
SO Microbes and Infection, (December, 2000) Vol. 2, No. 15, pp. 1799-1806. print.
ISSN: 1286-4579.
DT Article
LA English
ED Entered STN: 14 Mar 2001
Last Updated on STN: 15 Feb 2002
AB Viable antigen (Ag) delivery systems expressing defined pathogen-derived proteins represent powerful candidates for future vaccination strategies. Here, recombinant (r)Salmonella typhimurium aroA strains secreting listeriolysin (Hly) of Listeria monocytogenes in haemolytic or non-haemolytic form were constructed to direct these carriers into

cytosolic or phagosomal host cell compartments, respectively. Oral and intravenous (i.v.) vaccination of mice with either construct induced 'transporter associated with antigen processing'-dependent protection against the intracellular bacterial pathogen L. monocytogenes. Comparison of oral immunization with both rSalmonella constructs revealed superior vaccine efficacy of the haemolytic rS. typhimurium Hlys construct as compared to the non-haemolytic rSalmonella Hlys492 strain. In contrast, efficacy of i.v. vaccination with either rSalmonella strain did not significantly differ. Therefore, rSalmonella strains secreting biologically active Hly represent valuable delivery systems for heterologous rAg or DNA which should be exploited for future mucosal vaccination strategies.

L2 ANSWER 20 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 12
AN 2000:403329 BIOSIS
DN PREV200000403329
TI PCR-based quantification of Pneumocystis carinii in in vitro systems.
AU Hanano, Ralph; Fensterle, Joachim; Nusser, Petra; Reifenberg, Kurt; Kaufmann, Stefan H. E. [Reprint author]
CS Max-Planck-Institute for Infection-Biology, Monbijoustr. 2, 10117, Berlin, Germany
SO Microbes and Infection, (June, 2000) Vol. 2, No. 7, pp. 737-743. print. ISSN: 1286-4579.
DT Article
LA English
ED Entered STN: 20 Sep 2000
Last Updated on STN: 8 Jan 2002
AB In many laboratories, PCR has become a routine method for the sensitive diagnosis of Pneumocystis carinii in patient samples. In contrast, quantification of fungal numbers in in vitro setups still largely relies on more conventional procedures such as histological stainings. These are time consuming and their applications are limited when dealing with small fungal numbers contaminated with tissue and cellular debris. This study presents a sensitive and rapid method for P. carinii quantification based on PCR analysis that can be easily integrated into standard detection procedures without requiring any major additional steps. P. carinii-specific PCR performed with total DNA extracted from both standard samples with known fungal numbers and experimental samples was quantified relative to PCR products of a standard concentration from a control plasmid added prior to DNA extraction. This measure controlled for variations in DNA extraction and PCR efficiency among the samples to be compared. The correlation between analyzed P. carinii-specific DNA and the actual fungal numbers employed was highly significant.

L2 ANSWER 21 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:199968 BIOSIS
DN PREV200100199968
TI Cell-mediated immunity induced by recombinant M. bovis BCG strains expressing p60 of L. monocytogenes in different bacterial compartments: Importance of membrane-targeted display as lipoprotein derivative for vaccine efficacy.
AU Grode, L. [Reprint author]; Kursar, M. [Reprint author]; Fensterle, J. [Reprint author]; Kaufmann, S. H. E. [Reprint author]; Hess, J.
CS Abteilung Immunologie, Max-Planck-Institut fuer Infektionsbiologie, Berlin, Germany
SO Immunobiology, (November, 2000) Vol. 203, No. 1-2, pp. 318-319. print. Meeting Info.: Joint Annual Meeting of the German and Dutch Societies of Immunology. Duseldorf, Germany. November 29-December 02, 2000. CODEN: IMMND4. ISSN: 0171-2985.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English

ED Entered STN: 25 Apr 2001
Last Updated on STN: 18 Feb 2002

L2 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 13
AN 1999:673662 CAPLUS
DN 131:350061
TI Effective DNA vaccination against listeriosis by prime/boost inoculation with the gene gun
AU Fensterle, Joachim; Grode, Leander; Hess, Jurgen; Kaufmann, Stefan H. E.
CS Department of Immunology, Max-Planck-Institute for Infection Biology, Berlin, D-10117, Germany
SO Journal of Immunology (1999), 163(8), 4510-4518
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Protective immunity against Listeria monocytogenes strongly depends on CD8+ T lymphocytes, and both IFN-γ secretion and target cell killing are considered relevant to protection. The authors analyzed whether they could induce a protective type 1 immune response by DNA vaccination with the gene gun using plasmids encoding for 2 immunodominant listerial antigens, listeriolysin and p60. To induce a Th1 response, the authors (1) copptd. a plasmid encoding for GM-CSF, (2) employed a prime/boost vaccination schedule with a 45-day interval, and (3) co-injected oligodeoxynucleotides (ODN) containing immunostimulatory CpG motifs. DNA immunization of BALB/c mice with plasmids encoding for listeriolysin (pChly) and p60 (pCiap) efficiently induced MHC class I-restricted, Ag-specific CD8+ T cells that produced IFN-γ. Co-injection of CpG-ODN increased the frequency of specific IFN-γ-secreting T cells. Although pChly induced specific CD8+ T cells expressing CTL activity, it failed to stimulate CD4+ T cells. Only pCiap induced CD4+ T cell and humoral responses, which were predominantly of Th2 type. Vaccination with either plasmid induced protective immunity against listerial challenge, and co-injection of CpG ODN improved vaccine efficacy in some situations. This study demonstrates the feasibility of gene gun administration of plasmid DNA for inducing immunity against an intracellular pathogen for which protection primarily depends on type 1 CD8+ T cells.
RE.CNT 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 23 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 14
AN 2000:106668 BIOSIS
DN PREV200000106668
TI The need for a novel generation of vaccines.
AU Kaufmann, Stefan H. E. [Reprint author]; Fensterle, Joachim; Hess, Juergen
CS Depart. of Immunology, Max-Planck-Institute of Infection Biology, Monbijoustr. 2, D-10117, Berlin, Germany
SO Immunobiology, (Dec., 1999) Vol. 201, No. 2, pp. 272-282. print.
CODEN: IMMND4. ISSN: 0171-2985.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 22 Mar 2000
Last Updated on STN: 3 Jan 2002
AB Although empirical vaccine development was highly successful, it has now reached its limits. Vaccines are only efficacious against those pathogens which are primarily controlled by antibodies. Protection against many infectious agents, however, strongly depends on T lymphocytes. Thus, novel vaccines have to stimulate the combination of T lymphocytes that is required for an optimum protective immune response. Although identification of antigens remains crucial, novel vaccine design also

needs to consider the best way of introducing these antigens to the immune system. Intracellular antigen compartmentalisation, the early cytokine milieu and the appropriate surface expression of co-stimulatory molecules are of major relevance for understanding how novel vaccines could induce a protective immune response mediated by T lymphocytes. Intracellular bacteria are controlled by T lymphocytes and efficacious vaccines against these pathogens are not available yet. In this treatise, two experimental vaccination strategies will be described in more detail. These encompass recombinant vaccine carriers expressing, and naked DNA constructs encoding, heterologous antigens. Both vaccination strategies proved to be protective in the model of experimental listeriosis of mice.

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E2            2     GOEBEL WEMER/AU
E3          484 --> GOEBEL WERNER/AU
E4            4     GOEBEL WIEBKE/AU
E5            1     GOEBEL WILH/AU
E6           54     GOEBEL WILHELM/AU
E7            1     GOEBEL WILHELM K/AU
E8            1     GOEBEL WILLIAM A/AU
E9            5     GOEBEL WILLIAM K/AU
E10           6     GOEBEL WILLIAM KEITH/AU
E11           2     GOEBEL WILLIAM M/AU
E12           1     GOEBEL WILLIAM P/AU

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L3          102 ("GOEBEL WEMER"/AU OR "GOEBEL WERNER"/AU) AND VACCINE?

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PROCESSING COMPLETED FOR L3
L4           69 DUP REM L3 (33 DUPLICATES REMOVED)

=> s l4 and (mammalian cell?)
L5            5 L4 AND (MAMMALIAN CELL?)

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YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L5   ANSWER 1 OF 5  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
AN   2005:258647  BIOSIS
DN   PREV200510044779
TI   Bacterial delivery of functional messenger RNA to mammalian
     cells.
AU   Schoen, Christoph; Kolb-Maeurer, Annette; Geginat, Gernot; Loeffler,
     Daniela; Bergmann, Birgit; Stritzker, Jochen; Szalay, Aladar A.; Pilgrim,
     Sabine; Goebel, Werner [Reprint Author]
CS   Univ Wurzburg, Biozentrum, Lehrstuhl Mikrobiol, D-97074 Wurzburg, Germany
     goebel@biozentrum.uni-wuerzburg.de
SO   Cellular Microbiology, (MAY 2005) Vol. 7, No. 5, pp. 709-724.
     ISSN: 1462-5814.
DT   Article
LA   English
ED   Entered STN: 14 Jul 2005
     Last Updated on STN: 14 Jul 2005
AB   The limited access to the nuclear compartment may constitute one of the
     major barriers after bacteria-mediated expression plasmid DNA delivery to
     eukaryotic cells. Alternatively, a self-destructing Listeria
     monocytogenes strain was used to release translation-competent mRNA
     directly into the cytosol of epithelial cells, macrophages and human
     dendritic cells. Enhanced green fluorescent protein (EGFP)-encoding mRNA,
     adapted for translation in mammalian cells by linking
     an IRES element to the 5'-end of the egfp coding sequence, was produced by
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T7 RNA polymerase in the carrier bacteria upon entry into the cytosol where the mRNA is efficiently released from the lysed bacteria and immediately translated in eukaryotic host cells. Besides the much earlier expression of EGFP being detectable already 4 h after infection, the number of EGFP expressing mammalian cells obtained with this novel RNA delivery technique is comparable to or - especially in phagocytic cells - even higher than that obtained with the expression plasmid DNA delivery strategy. Accordingly, bacteria-mediated delivery of ovalbumin-encoding mRNA to macrophages resulted in efficient antigen processing and presentation in vitro indicating that this approach may also be adapted for the in vivo delivery of antigen-encoding mRNA leading to a more efficient immune response when applied to vaccine development.

L5 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2000:296977 BIOSIS
DN PREV200000296977
TI Yersinia enterocolitica-mediated translocation of defined fusion proteins to the cytosol of mammalian cells results in peptide-specific MHC class I-restricted antigen presentation.
AU Ruessmann, Holger [Reprint author]; Weissmueller, Astrid; Geginat, Gernot; Igwe, Emeka I.; Roggenkamp, Andreas; Bubert, Andreas; Goebel, Werner; Hof, Herbert; Heesemann, Juergen
CS Max von Pettenkofer-Institut fuer Hygiene und Medizinische Mikrobiologie, Ludwig Maximilians Universitaet Muenchen, Pettenkoferstr. 9a, D-80336, Muenchen, Germany
SO European Journal of Immunology, (May, 2000) Vol. 30, No. 5, pp. 1375-1384. print.
CODEN: EJIMAF. ISSN: 0014-2980.
DT Article
LA English
ED Entered STN: 12 Jul 2000
Last Updated on STN: 7 Jan 2002
AB Yersinia enterocolitica delivers a set of effector proteins (Yersinia outer proteins (Yop)) into the cytosol of target cells to modulate host cell signal transduction pathways required for the extracellular survival of the bacterium. Secretion and subsequent translocation of Yop across the eukaryotic cell membrane are achieved via a type III secretion system. About 50-100 amino acids of the N terminus of Yop are required for chaperone-directed secretion and translocation. In this study, it is demonstrated by immunoblot analysis of Yersinia-infected cultured epithelial cells that one ot these proteins, YopE, can serve as a molecular carrier to deliver protein fragments of the heterologous p60 antigen of Listeria monocytogenes into the cytosol of target cells. T cell activation assays revealed that the observed type III-mediated antigen translocation led to a p60 peptide-specific MHC class I-restricted antigen presentation. Efficient translocation and antigen presentation were strictly dependent on the co-localized expression of hybrid YopE-p60 proteins and the YopE-specific chaperone SycE. These results suggest that the Yersinia type III secretion system may serve as an attractive tool for antigen delivery in Yersinia-based live vaccines to induce cellular immune responses.

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:700618 CAPLUS
DN 139:290721
TI Transfer of eukaryotic expression plasmids to mammalian host cells by Gram-negative bacteria
AU Weiss, Siegfried; Chakraborty, Trinad
CS Molecular Immunology, GBF - German Research Centre for Biotechnology, Braunschweig, D-38124, Germany
SO Vaccine Delivery Strategies (2002), 289-314. Editor(s): Dietrich, Guido; Goebel, Werner. Publisher: Horizon Scientific Press, Wymondham, UK.

CODEN: 69ELHT; ISBN: 1-898486-48-4
DT Conference; General Review
LA English
AB A review. The concept of transkingdom transfer of DNA from bacteria to other organisms has recently been extended to include eucaryotic host cells. Attenuated intracellular bacteria or non-pathogenic bacteria equipped with adhesion and invasion properties have now been demonstrated to transfer eukaryotic expression plasmids to mammalian host cells in vitro and in vivo. Here, the authors review the use of Gram-neg. bacteria for induction of immune responses towards protein antigens encoded by the plasmid, their use to complement genetic defects or deliver immunotherapeutic proteins. Plasmid transfer is effected by bacterial death within the host cell usually resulting from metabolic attenuation. It is also possible that bacterial macromol. secretion machineries direct DNA transfer to the infected host cell. Plasmid transfer has been reported for Shigella flexneri, Salmonella typhimurium and S. typhi, S. choleraesuis, Yersinia pseudotuberculosis and Escherichia coli, but clearly this property can be extended to include any bacterial species as has recently been demonstrated with Agrobacterium tumefaciens. Gene transfer in vivo attempts were mainly directed towards vaccination strategies using Shigella and Salmonella as carrier where this type of immunization was more efficacious than either direct application of antigen, using the same bacterium as a heterologous carrier expressing the antigen via a prokaryotic promoter, or vaccination with naked DNA. The efficacy of induction of protective immune responses by such DNA carriers and ease of generating these vehicles for gene transfer using technol. validated for mass vaccination programs makes this a highly attractive area for further research and development.
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:697071 CAPLUS
DN 139:224411
TI Transgenic microorganisms producing cell antigens for use as vaccines, especially tumor vaccines
IN Rapp, Ulf R.; Goebel, Werner; Gentschev, Ivaylo; Fensterle, Joachim
PA Medinnova Gesellschaft fuer Medizinische Innovationen aus Akademischer Forschung m.b.H., Germany
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003072789 | A2 | 20030904 | WO 2003-DE471 | 20030213 |
| WO 2003072789 | A3 | 20040212 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10208653 | A1 | 20030918 | DE 2002-10208653 | 20020228 |
| CA 2513190 | A1 | 20030904 | CA 2003-2513190 | 20030213 |
| AU 2003206664 | A1 | 20030909 | AU 2003-206664 | 20030213 |
| EP 1478756 | A2 | 20041124 | EP 2003-704315 | 20030213 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

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| | JP 2005518795 | T | 20050630 | JP 2003-571470 | 20030213 |
| | CN 1650014 | A | 20050803 | CN 2003-809598 | 20030213 |
| | NO 2004003926 | A | 20040920 | NO 2004-3926 | 20040920 |
| | IN 2004KN01389 | A | 20060526 | IN 2004-KN1389 | 20040920 |
| | US 2006105423 | A1 | 20060518 | US 2005-506096 | 20050611 |
| PRAI | DE 2002-10208653 | A | 20020228 | | |
| | WO 2003-DE471 | W | 20030213 | | |

AB The invention relates to a microorganism expressing a chimeric gene encoding a cell antigen. The chimeric gene comprises (1) a sequence coding for at least one epitope of a tumor antigen and/or of an antigen specific for the tissue from which the tumor originates; (2) an optional sequence coding for a protein that stimulates cells of the immune system; (3a) a sequence coding for a transport system which makes it possible to secrete or display on the microbial surface the chimeric gene product; and/or (3b) a sequence encoding a protein used for lysing the microorganisms in the cytosol of mammalian cells and for intracellularly releasing plasmids which are contained in the lysed microorganisms; and (4) a promoter for expressing the chimeric gene which is capable of being activated in the microorganism, is tissue--specific but not cell-specific. Also disclosed is the use of such microorganisms as tumor vaccines. Thus, c-raf-expressing transgenic mice were orally immunized with attenuated Salmonella typhimurium containing plasmid pMO-Raf. This plasmid contains a chimeric gene consisting of human c-Raf cDNA fused to hlyA. This immunization overcame the self-tolerance of C-Raf and led to a CD4+ T cell response. The lung tumor mass in these mice was less than that in control mice.

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:464109 CAPLUS
DN 131:83981
TI Delivery of polypeptide-encoding plasmid DNA into the cytosol of macrophages by attenuated suicide bacteria for gene therapy and vaccination purposes
IN Goebel, Werner
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9934007 | A1 | 19990708 | WO 1998-EP8345 | 19981218 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 6143551 | A | 20001107 | US 1997-999391 | 19971229 |
| | CA 2317111 | A1 | 19990708 | CA 1998-2317111 | 19981218 |
| | AU 9920547 | A | 19990719 | AU 1999-20547 | 19981218 |
| | AU 753888 | B2 | 20021031 | | |
| | BR 9814546 | A | 20001010 | BR 1998-14546 | 19981218 |
| | EP 1042495 | A1 | 20001011 | EP 1998-965287 | 19981218 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | HU 200100994 | A2 | 20010730 | HU 2001-994 | 19981218 |
| | HU 200100994 | A3 | 20031028 | | |
| | JP 2002500017 | T | 20020108 | JP 2000-526662 | 19981218 |
| | US 2002045587 | A1 | 20020418 | US 2000-532964 | 20000322 |

PRAI US 1997-999391 A 19971229
WO 1998-EP8345 W 19981218
AB The invention relates to the introduction of DNA or RNA sequences into a mammalian cell to achieve controlled expression of a polypeptide. This is carried out by infecting a mammalian host cell with an attenuated invasive intracellular bacterium transformed with a promoter which is activated in the cytosol of the host cell and activates the expression of the gene encoding a polypeptide which has therapeutic properties. The polypeptide can be a bacteriophage lysine, which when released into the cytosol causes autolysis of the bacterium. The invention is useful in gene therapy, vaccination, and any therapeutic situation in which a polypeptide should be administered to a host or cells of said host, as well as for the production of polypeptides by mammalian cells, e.g., in culture or in transgenic animals.
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> e rapp ulf r/au
E1 51 RAPP ULF/AU
E2 1 RAPP ULF F/AU
E3 402 --> RAPP ULF R/AU
E4 2 RAPP ULF RUDIGER/AU
E5 1 RAPP ULF RUEDIGER/AU
E6 2 RAPP ULI/AU
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E9 3 RAPP URSULA/AU
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=> s e2-e3 and (mammalian cell?)
L6 13 ("RAPP ULF F"/AU OR "RAPP ULF R"/AU) AND (MAMMALIAN CELL?)

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 8 DUP REM L6 (5 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2004:450236 BIOSIS
DN PREV200400449850
TI Dynamic changes in C-raf phosphorylation and 14-3-3 protein binding in response to growth factor stimulation - Differential roles of 14-3-3 protein binding sites.
AU Hekman, Mirko; Wiese, Stefan; Metz, Renate; Albert, Stefan; Troppmair, Jakob; Nickel, Joachim; Sendtner, Michael; Rapp, Ulf R. [Reprint Author]
CS Inst Med Radiat and Cell Res, Univ Wuerzburg, D-97078, Wuerzburg, Germany rappur@mail.uni-wuerzburg.de
SO Journal of Biological Chemistry, (April 2 2004) Vol. 279, No. 14, pp. 14074-14086. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 24 Nov 2004
Last Updated on STN: 24 Nov 2004
AB Phosphorylation events play a crucial role in Raf activation. Phosphorylation of serines 259 and 621 in C-Raf and serines 364 and 728 in

B-Raf has been suggested to be critical for association with 14-3-3 proteins. To study the functional consequences of Raf phosphorylations at these positions, we developed and characterized phosphospecific antibodies directed against 14-3-3 binding epitopes: a monoclonal phosphospecific antibody (6B4) directed against pS621 and a polyclonal antibody specific for B-Raf-pS364 epitope. Although 6B4 detected both C- and B-Raf in Western blots, it specifically recognizes the native form of C- Raf but not B-Raf. Contrary to B-Raf, a kinase-dead mutant of C- Raf was found to be only poorly phosphorylated in the Ser-621 position. Moreover, serine 259 to alanine mutation prevented the Ser-621 phosphorylation suggesting an interdependence between these two 14-3-3 binding domains. Direct C-Raf cntdot 14-3-3 binding studies with purified proteins combined with competition assays revealed that the 14-3-3 binding domain surrounding pS621 represents the high affinity binding site, whereas the pS259 epitope mediates lower affinity binding. Raf isozymes differ in their 14-3-3 association rates. The time course of endogenous C- Raf activation in mammalian cells by nerve growth factor (NGF) has been examined using both phosphospecific antibodies directed against 14-3-3 binding sites (6B4 and anti-pS259) as well as phosphospecific antibodies directed against the activation domain (anti-pS338 and anti-pY340/pY341). Time course of Ser-621 phosphorylation, in contrast to Ser-259 phosphorylation, exhibited unexpected pattern reaching maximal phosphorylation within 30 s of NGF stimulation. Phosphorylation of tyrosine 340/341 reached maximal levels subsequent to Ser-621 phosphorylation and was coincident with emergence of kinase activity. Taken together, we found substantial differences between C- Raf cntdot 14-3-3 binding epitopes pS259 and pS621 and visualized for the first time the sequence of the essential C- Raf phosphorylation events in mammalian cells in response to growth factor stimulation.

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:697071 CAPLUS
DN 139:224411
TI Transgenic microorganisms producing cell antigens for use as vaccines, especially tumor vaccines
IN Rapp, Ulf R.; Goebel, Werner; Gentschev, Ivaylo; Fensterle, Joachim
PA Medinnova Gesellschaft fuer Medizinische Innovationen aus Akademischer Forschung m.b.H., Germany
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003072789 | A2 | 20030904 | WO 2003-DE471 | 20030213 |
| | WO 2003072789 | A3 | 20040212 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | DE 10208653 | A1 | 20030918 | DE 2002-10208653 | 20020228 |
| | CA 2513190 | A1 | 20030904 | CA 2003-2513190 | 20030213 |
| | AU 2003206664 | A1 | 20030909 | AU 2003-206664 | 20030213 |
| | EP 1478756 | A2 | 20041124 | EP 2003-704315 | 20030213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

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| | JP 2005518795 | T | 20050630 | JP 2003-571470 | 20030213 |
| | CN 1650014 | A | 20050803 | CN 2003-809598 | 20030213 |
| | NO 2004003926 | A | 20040920 | NO 2004-3926 | 20040920 |
| | IN 2004KN01389 | A | 20060526 | IN 2004-KN1389 | 20040920 |
| | US 2006105423 | A1 | 20060518 | US 2005-506096 | 20050611 |
| PRAI | DE 2002-10208653 | A | 20020228 | | |
| | WO 2003-DE471 | W | 20030213 | | |

AB The invention relates to a microorganism expressing a chimeric gene encoding a cell antigen. The chimeric gene comprises (1) a sequence coding for at least one epitope of a tumor antigen and/or of an antigen specific for the tissue from which the tumor originates; (2) an optional sequence coding for a protein that stimulates cells of the immune system; (3a) a sequence coding for a transport system which makes it possible to secrete or display on the microbial surface the chimeric gene product; and/or (3b) a sequence encoding a protein used for lysing the microorganisms in the cytosol of mammalian cells and for intracellularly releasing plasmids which are contained in the lysed microorganisms; and (4) a promoter for expressing the chimeric gene which is capable of being activated in the microorganism, is tissue--specific but not cell-specific. Also disclosed is the use of such microorganisms as tumor vaccines. Thus, c-raf-expressing transgenic mice were orally immunized with attenuated Salmonella typhimurium containing plasmid pMO-Raf. This plasmid contains a chimeric gene consisting of human c-Raf cDNA fused to hlyA. This immunization overcame the self-tolerance of C-Raf and led to a CD4+ T cell response. The lung tumor mass in these mice was less than that in control mice.

L7 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2
AN 1999:455370 BIOSIS
DN PREV199900455370
TI Binding of Gbetagamma subunits to cRaf1 downregulates G-protein-coupled receptor signalling.
AU Slupsky, Joseph R.; Quitterer, Ursula; Weber, Christoph K.; Gierschik, Peter; Lohse, Martin J.; Rapp, Ulf R. [Reprint author]
CS Abteilung fuer Naturheilkunde und Klinische Pharmakologie, Universitaet Ulm, Helmholtzstrasse 20, D-89081, Ulm, Germany
SO Current Biology, (Sept. 9, 1999) Vol. 9, No. 17, pp. 971-974. print.
CODEN: CUBLE2. ISSN: 0960-9822.
DT Article
LA English
ED Entered STN: 1 Nov 1999
Last Updated on STN: 1 Nov 1999
AB Receptors of the seven transmembrane domain family are coupled to heterotrimeric G proteins (1). Binding of ligand to these receptors induces dissociation of the heterotrimeric complex into free GTP-Galpha and Gbetagamma subunits, which then interact with their respective effector molecules to stimulate specific cellular responses. In some cases, these cellular responses involve mitogenic signalling (2). The mitogen-activated protein (MAP) kinase cascade is initiated by the protein kinase cRaf1 and links growth factor receptor signalling to cell growth and differentiation (3). The main activator of cRaf1 is the small GTP-binding protein Ras (4), and the binding of cRaf1 to GTP-Ras translocates cRaf1 to the plasma membrane, where it is activated (5). It has been reported that cRaf1 associates directly with the beta subunit of heterotrimeric G proteins in vitro, and with the betagamma subunit complex in vivo (6), but the role of this association is not yet understood. Here, we show that cRaf1 associates with Gbeta1gamma2, and that this association in mammalian cells is significantly enhanced when active p21Ras is present or when cRaf1 is otherwise targeted to the membrane. Association with Gbeta1gamma2 has no effect on the kinase activity of cRaf1, but cRaf1 can affect Gbetagamma-mediated signalling events. Thus, membrane-localised cRaf1 inhibits

G-protein-coupled receptor (GPCR)-stimulated activation of phospholipase Cbeta (PLCbeta) by sequestration of Gbetagamma subunits, an effect also observed with endogenous levels of cRaf1. Our data suggest that cRaf1 may be an important regulator of signalling by Gbetagamma, particularly in those GPCR systems that stimulate the MAP kinase cascade through the activation of p21Ras.

L7 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 3
AN 1996:481609 BIOSIS
DN PREV199699196865
TI Bcl-2 interacting protein, BAG-1, binds to and activates the kinase Raf-1.
AU Wang, Hong-Gang; Takayama, Shinichi; Rapp, Ulf R.; Reed, John C.
CS Burnham Inst., 10901 North Torrey Pines Road, La Jolla, CA 92037, USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1996) Vol. 93, No. 14, pp. 7063-7068.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English
ED Entered STN: 24 Oct 1996
Last Updated on STN: 10 Dec 1996
AB The Bcl-2 protein blocks programmed cell death (apoptosis) through an unknown mechanism. Previously we identified a Bcl-2 interacting protein BAG-1 that enhances the anti-apoptotic effects of Bcl-2. Like BAG-1, the serine/threonine protein kinase Raf-I also can functionally cooperate with Bcl-2 in suppressing apoptosis. Here we show that Raf-1 and BAG-1 specifically interact in vitro and in yeast two-hybrid assays. Raf-1 and BAG-1 can also be coimmuno-precipitated from mammalian cells and from insect cells infected with recombinant baculoviruses encoding these proteins. Furthermore, bacterially-produced BAG-1 protein can increase the kinase activity of Raf-1 in vitro. BAG-1 also activates this mammalian kinase in yeast. These observations suggest that the Bcl-2 binding protein BAG-1 joins Ras and 14-3-3 proteins as potential activators of the kinase Raf-1.

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:291406 CAPLUS
DN 120:291406
TI Mitogen-activated protein kinase/extracellular signal-regulated protein kinase activation by oncogenes, serum, and 12-O-tetradecanoylphorbol-13-acetate requires Raf and is necessary for transformation
AU Troppmair, Jakob; Bruder, Joseph T.; Munoz, Hildita; Lloyd, Patricia A.; Kyriakis, John; Banerjee, Papia; Avruch, Joseph; Rapp, Ulf R.
CS Viral Pathol. Sect., Lab. Viral Carcinog., Frederick, MD, 21702-1201, USA
SO Journal of Biological Chemistry (1994), 269(9), 7030-5
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The protein kinase cascade Raf-MAPKK/MEK-MAPK/ERK connects protein tyrosine kinase receptors in the membrane with control of transcription factor activity in the nucleus. The authors have examined whether Raf is obligatory for activation of this cascade and whether this signaling pathway is relevant to transformation. By use of transient assays with epitope-tagged ERK-1 cDNA and a dominant inhibitory mutant of Raf-1 the authors found that serum and 12-O-tetradecanoylphorbol-13-acetate as well as representatives of three classes of oncogenes (protein tyrosine kinases abl/src, Ras, and protein serine/threonine kinases mos/cot) were all Raf-dependent for stimulation of MAPK. All of the MAPK stimulating oncogenes were also activators of Raf kinase as judged by shift induction. It thus appears that there is little or no redundancy in pathways used by growth regulators for activation of MAPK/ERK. Furthermore, the ability to stimulate MAPK/ERK appears to be critical for transformation by oncogenic Raf-1 as ERK-1 and -2 synergized with v-raf in a focus induction assay on NIH3T3 cells and kinase dead mutants of ERK-2 were inhibitory. Raf/ERK

synergism was also observed in transcriptional transactivation of the oncogene-response element in the polyoma enhancer. It was concluded that this Raf signaling pathway, which connects to many upstream activators and downstream effectors, is essential for transformation by most oncogenes.

L7 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 4
AN 1993:431727 BIOSIS
DN PREV199396086352
TI Identification of the major phosphorylation sites of the Raf-1 kinase.
AU Morrison, Deborah K. [Reprint author]; Heidecker, Gisela; Rapp, Ulf R.; Copeland, Terry D.
CS ABL-Basic Research Program, Lab. Viral Carcinogenesis, National Cancer Inst.-Frederick Cancer Research Development Center, Frederick, MD 21702, USA
SO Journal of Biological Chemistry, (1993) Vol. 268, No. 23, pp. 17309-17316.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 22 Sep 1993
Last Updated on STN: 3 Jan 1995
AB Treatment of cells with various growth factors and mitogens results in the rapid hyperphosphorylation and activation of the Raf-1 kinase. To determine if phosphorylation events affect Raf-1 activity, we have initiated experiments to identify the phosphorylation sites of Raf-1. In this report, we find that Ser-43, Ser-259, and Ser-621 are the major sites of Raf-I which are phosphorylated in mammalian cells
and in Sf9 insect cells infected with a recombinant baculovirus encoding human Raf-1. Mutant Raf-1 proteins lacking kinase activity are also phosphorylated on these sites in vivo, indicating that these phosphorylation events are not a consequence of autophosphorylation. Furthermore, we find that Thr-268 is the predominant Raf-1 residue phosphorylated in in vitro autokinase assays. In addition, we have examined the biochemical activity of baculovirus-expressed Raf-1 proteins containing mutations at these phosphorylation sites. In in vitro protein kinase assays Ser-259 mutant proteins were 2-fold more active than wild-type Raf-1 and Ser-621 mutant proteins were inactive as kinases. Analysis of the residues surrounding Ser-259 and Ser-621 indicates that RSXSXP may be a consensus sequence for the kinase responsible for phosphorylation of Raf-1 at these sites. Interestingly, these RSXSXP sequences are completely conserved throughout evolution in all Raf family members.

L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1986:603937 CAPLUS
DN 105:203937
TI Recombinant murine retroviruses containing avian v-myc induce a wide spectrum of neoplasms in newborn mice
AU Morse, Herbert C., III; Hartley, Janet W.; Fredrickson, Torgny N.; Yetter, Robert A.; Majumdar, Chirabrata; Cleveland, John L.; Rapp, Ulf R.
CS Lab. Immunopathol., Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 20892, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1986), 83(18), 6868-72
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB NFS/N mice infected within 48 h of birth with pseudotypes of recombinant murine leukemia viruses containing avian v-myc, developed T-cell, pre-B-cell, and B-cell lymphomas and epithelial tumors including pancreatic and mammary adenocarcinomas. Primary hematopoietic and epithelial tumors and continuous in vitro cell lines derived from some of these tumors, established in the absence of added growth factors, exhibited clonal integrations of v-myc and expressed v-myc RNA. These results show that

deregulated expression of the myc oncogene in mammalian cells can initiate a wide variety of neoplasms.

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1983:140198 CAPLUS
DN 98:140198
TI New mammalian transforming retrovirus: demonstration of a polyprotein gene product
AU Rapp, Ulf R.; Reynolds, Fred H., Jr.; Stephenson, John R.
CS Lab. Viral Carcinogen., Natl. Cancer Inst., Frederick, MD, 21701, USA
SO Journal of Virology (1983), 45(3), 914-24
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB A new acute transforming type C retrovirus was isolated from mice inoculated with a virus stock obtained by iododeoxyuridine induction of methylcholanthrene-transformed C3H/10T1/2 mouse cells. This virus, designated 3611-MSV, transforms embryo fibroblasts and epithelial cells in culture and induces fibrosarcomas in vivo. Virus 3611-MSV is replication-defective and requires a type C helper virus for propagation both in vitro and in vivo. By using endpoint transmission of 3611-mSV to MMCE C17 mouse and FRE 3A rat cells, several nonproductively transformed clonal cell lines have been derived. Pseudotype virus stocks obtained from such clones transform cells in vitro, are highly oncogenic in vivo, and exhibit host range and serol. properties that are characteristic of their helper virus component. Examination of viral antigen expression in 3611-MSV-transformed cells has led to the demonstration of a 90,000-mol.-weight (Mr) polyprotein and a 75,000-Mr probable cleavage product, both containing the N-terminal murine leukemia virus gag gene proteins p15 and p12. In contrast to gene products of many previously described mammalian transforming viruses, 3611-MSV-encoded polyproteins lack detectable protein kinase activity, and 3611-MSV-transformed cells resemble chemical transformed cell line C3H/MCA-5, from which 3611-MuLV was originally derived, in that they do not exhibit elevated levels of phosphotyrosine. By mol. hybridization, the 3611-MSV transforming gene was shown to be distinct from previously previously described mammalian cellular oncogenic sequences, including c-ras, c-abl, c-fes, c-fms, c-sis, and c-mos.

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E7            1     STRITZKO TOMAS/AU
E8            1     STRITZKO WILHELM/AU
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L8            4 ("STRITZKER J"/AU OR "STRITZKER JOCHEN"/AU) AND (MAMMALIAN CELL?
                ) AND VACCINE?

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L9 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2005:258647 BIOSIS
DN PREV200510044779
TI Bacterial delivery of functional messenger RNA to mammalian cells.
AU Schoen, Christoph; Kolb-Maeurer, Annette; Geginat, Gernot; Loeffler, Daniela; Bergmann, Birgit; Stritzker, Jochen; Szalay, Aladar A.; Pilgrim, Sabine; Goebel, Werner [Reprint Author]
CS Univ Wurzburg, Biozentrum, Lehrstuhl Mikrobiol, D-97074 Wurzburg, Germany
goebel@biozentrum.uni-wuerzburg.de
SO Cellular Microbiology, (MAY 2005) Vol. 7, No. 5, pp. 709-724.
ISSN: 1462-5814.
DT Article
LA English
ED Entered STN: 14 Jul 2005
Last Updated on STN: 14 Jul 2005
AB The limited access to the nuclear compartment may constitute one of the major barriers after bacteria-mediated expression plasmid DNA delivery to eukaryotic cells. Alternatively, a self-destructing Listeria monocytogenes strain was used to release translation-competent mRNA directly into the cytosol of epithelial cells, macrophages and human dendritic cells. Enhanced green fluorescent protein (EGFP)-encoding mRNA, adapted for translation in mammalian cells by linking an IRES element to the 5'-end of the egfp coding sequence, was produced by T7 RNA polymerase in the carrier bacteria upon entry into the cytosol where the mRNA is efficiently released from the lysed bacteria and immediately translated in eukaryotic host cells. Besides the much earlier expression of EGFP being detectable already 4 h after infection, the number of EGFP expressing mammalian cells obtained with this novel RNA delivery technique is comparable to or - especially in phagocytic cells - even higher than that obtained with the expression plasmid DNA delivery strategy. Accordingly, bacteria-mediated delivery of ovalbumin-encoding mRNA to macrophages resulted in efficient antigen processing and presentation in vitro indicating that this approach may also be adapted for the in vivo delivery of antigen-encoding mRNA leading to a more efficient immune response when applied to vaccine development.

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E11 1 SCHMIDT ANDREAS M/AU
E12 1 SCHMIDT ANDREAS P/AU

=> e gentschev ivaylo/au
E1 1 GENTSCHEV GUIDO VV DIETRICHO/AU
E2 134 GENTSCHEV I/AU
E3 79 --> GENTSCHEV IVAYLO/AU
E4 11 GENTSCHEV IVO/AU
E5 1 GENTSCHEV J/AU
E6 1 GENTSCHEV P/AU
E7 26 GENTSCHEV PAVEL/AU
E8 10 GENTSCHEV T/AU
E9 2 GENTSCHEV T H/AU

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E10          1     GENTSCHEV TENTSCHO/AU
E11          1     GENTSCHEV VVAYLO HANS MOLLENKOPF/AU
E12          1     GENTSCHEV VVAYLO ZELJKA SOKOLOVIC/AU

=> s e2-e3 and (mammalian cell?) and vaccine?
L10          1 ("GENTSCHEV I"/AU OR "GENTSCHEV IVAYLO"/AU) AND (MAMMALIAN CELL?
               ) AND VACCINE?

=> d

L10  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2003:697071  CAPLUS
DN   139:224411
TI   Transgenic microorganisms producing cell antigens for use as
     vaccines, especially tumor vaccines
IN   Rapp, Ulf R.; Goebel, Werner; Gentschev, Ivaylo; Fensterle,
     Joachim
PA   Medinnova Gesellschaft fuer Medizinische Innovationen aus Akademischer
     Forschung m.b.H., Germany
SO   PCT Int. Appl., 29 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2003072789         A2    20030904    WO 2003-DE471           20030213
     WO 2003072789         A3    20040212
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     DE 10208653           A1    20030918    DE 2002-10208653        20020228
     CA 2513190            A1    20030904    CA 2003-2513190         20030213
     AU 2003206664         A1    20030909    AU 2003-206664          20030213
     EP 1478756            A2    20041124    EP 2003-704315          20030213
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2005518795         T     20050630    JP 2003-571470          20030213
     CN 1650014            A     20050803    CN 2003-809598          20030213
     NO 2004003926         A     20040920    NO 2004-3926            20040920
     IN 2004KN01389        A     20060526    IN 2004-KN1389          20040920
     US 2006105423         A1    20060518    US 2005-506096          20050611
PRAI DE 2002-10208653      A     20020228
     WO 2003-DE471         W     20030213


=> e potapenko tamara/au
E1           2     POTAPENKO T L/AU
E2           3     POTAPENKO T S/AU
E3           7 --> POTAPENKO TAMARA/AU
E4           2     POTAPENKO V/AU
E5          89     POTAPENKO V A/AU
E6           1     POTAPENKO V D/AU
E7          34     POTAPENKO V E/AU
E8           1     POTAPENKO V G/AU
E9           1     POTAPENKO V I/AU
E10          3     POTAPENKO V M/AU
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E11          10      POTAPENKO V N/AU
E12           1      POTAPENKO V P/AU

=> s e3
L11           7 "POTAPENKO TAMARA"/AU

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12           5 DUP REM L11 (2 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L12  ANSWER 1 OF 5     MEDLINE on STN
AN   2005090722     MEDLINE
DN   PubMed ID: 15703070
TI   Use of a recombinant Salmonella enterica serovar Typhimurium strain
     expressing C-Raf for protection against C-Raf induced lung adenoma in
     mice.
AU   Gentschev Ivaylo; Fensterle Joachim; Schmidt Andreas; Potapenko
     Tamara; Troppmair Jakob; Goebel Werner; Rapp Ulf R
CS   Institut fur Medizinische Strahlenkunde und Zellforschung (MSZ),
     University of Wuerzburg, D-97078 Wuerzburg, Germany..
     ivaylo.gentschev@mail.uni-wuerzburg.de
SO   BMC cancer, (2005 Feb 9) Vol. 5, pp. 15.  Electronic Publication:
     2005-02-09.
     Journal code: 100967800. E-ISSN: 1471-2407.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA   English
FS   Priority Journals
EM   200510
ED   Entered STN: 23 Feb 2005
     Last Updated on STN: 18 Oct 2005
     Entered Medline: 17 Oct 2005
AB   BACKGROUND: Serine-threonine kinases of the Raf family (A-Raf, B-Raf,
     C-Raf) are central players in cellular signal transduction, and thus often
     causally involved in the development of cancer when mutated or
     over-expressed.  Therefore these proteins are potential targets for
     immunotherapy and a possible basis for vaccine development against tumors.
     In this study we analyzed the functionality of a new live C-Raf vaccine
     based on an attenuated Salmonella enterica serovar Typhimurium aroA strain
     in two Raf dependent lung tumor mouse models.  METHODS: The antigen C-Raf
     has been fused to the C-terminal secretion signal of Escherichia coli
     alpha-hemolysin and expressed in secreted form by an attenuated aroA
     Salmonella enterica serovar Typhimurium strain via the alpha-hemolysin
     secretion pathway.  The effect of the immunization with this recombinant
     C-Raf strain on wild-type C57BL/6 or lung tumor bearing transgenic BxB
     mice was analyzed using western blot and FACS analysis as well as specific
     tumor growth assays.  RESULTS: C-Raf antigen was successfully expressed in
     secreted form by an attenuated Salmonella enterica serovar Typhimurium
     aroA strain using the E. coli hemolysin secretion system.  Immunization of
     wild-type C57BL/6 or tumor bearing mice provoked specific C-Raf antibody
     and T-cell responses.  Most importantly, the vaccine strain significantly
     reduced tumor growth in two transgenic mouse models of Raf
     oncogene-induced lung adenomas.  CONCLUSIONS: The combination of the C-Raf
     antigen, hemolysin secretion system and Salmonella enterica serovar
     Typhimurium could form the basis for a new generation of live bacterial
     vaccines for the treatment of Raf dependent human malignancies.

L12  ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN  DUPLICATE 1
AN   2005:240459  CAPLUS
DN   142:390617
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TI Use of a recombinant Salmonella enterica serovar Typhimurium strain expressing C-Raf for protection against C-Raf induced lung adenoma in mice
AU Gentschev, Ivaylo; Fensterle, Joachim; Schmidt, Andreas; Potapenko, Tamara; Troppmair, Jakob; Goebel, Werner; Rapp, Ulf R.
CS Institut fuer Medizinische Strahlenkunde und Zellforschung (MSZ), University of Wuerzburg, Wuerzburg, D-97078, Germany
SO BMC Cancer (2005), 5, No pp. given
CODEN: BCMACL; ISSN: 1471-2407
URL: http://www.biomedcentral.com/content/pdf/1471-2407-5-15.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Serine-threonine kinases of the Rat family (A-Raf, B-Raf, C-Raf) are central players in cellular signal transduction, and thus often causally involved in the development of cancer when mutated or over-expressed. Therefore, these proteins are potential targets for immunotherapy and a possible basis for vaccine development against tumors. In this study we analyzed the functionality of a new live C-Raf vaccine based on an attenuated Salmonella enterica serovar Typhimurium AroA strain in two Raf dependent lung tumor mouse models. The antigen C-Raf has been fused to the C-terminal secretion signal of Escherichia coli α-hemolysin and expressed in secreted form by an attenuated aroA Salmonella enterica serovar Typhimurium strain via the α-hemolysin secretion pathway. The effect of the immunization with this recombinant C-Raf strain on wild-type C57BL/6 or lung tumor bearing transgenic BxB mice was analyzed using western blot and FACS anal. as well as specific tumor growth assays. C-Raf antigen was successfully expressed in secreted form by an attenuated Salmonella enterica serovar Typhimurium aroA strain using the E. coli hemolysin secretion system. Immunization of wild-type C57BL/6 or tumor bearing mice provoked specific C-Raf antibody and T-cell responses. Most importantly, the vaccine strain significantly reduced tumor growth in two transgenic mouse models of Raf oncogene-induced lung adenomas. The combination of the C-Raf antigen, hemolysin secretion system and Salmonella enterica serovar Typhimurium could form the basis for a new generation of live bacterial vaccines for the treatment of Raf dependent human malignancies.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1080811 CAPLUS
DN 142:22299
TI Cells used as carriers for bacteria in the therapy of cancer and other diseases
IN Fensterle, Joachim; Goebel, Werner; Rapp, Ulf; Strizker, Jochen; Schmidt, Andreas; Gentschev, Ivaylo; Potapenko, Tamara
PA Medinnova Gesellschaft fuer Innovationen aus Akademischer Forschung m.b.H., Germany
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2004108155 | A1 | 20041216 | WO 2004-DE1178 | 20040607 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| DE | 10326187 | A1 | 20050105 | DE 2003-10326187 | 20030606 |
| AU | 2004244701 | A1 | 20041216 | AU 2004-244701 | 20040607 |
| CA | 2526789 | A1 | 20041216 | CA 2004-2526789 | 20040607 |
| EP | 1631310 | A1 | 20060308 | EP 2004-738631 | 20040607 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| CN | 1802175 | A | 20060712 | CN 2004-80015761 | 20040607 |
| BR | 2004011210 | A | 20060718 | BR 2004-11210 | 20040607 |
| JP | 2006526396 | T | 20061124 | JP 2006-508123 | 20040607 |
| IN | 2005MN01351 | A | 20060519 | IN 2005-MN1351 | 20051202 |
| NO | 2006000095 | A | 20060303 | NO 2006-95 | 20060106 |
| US | 2006240038 | A1 | 20061026 | US 2006-559663 | 20060621 |
| PRAI DE | 2003-10326187 | A | 20030606 | | |
| WO | 2004-DE1178 | W | 20040607 | | |

AB The invention relates to the use of a cell, which is charged with a microorganism that contains foreign DNA, in particular a bacterial microorganism, to produce a pharmaceutical composition Preferably, the foreign DNA codes for a defined active agent and the pharmaceutical composition is designed for use in the prophylaxis or treatment of a disease that can be treated with said active agent.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 MEDLINE on STN
AN 2004478998 MEDLINE
DN PubMed ID: 15361259
TI B-Raf specific antibody responses in melanoma patients.
AU Fensterle Joachim; Becker Jurgen C; Potapenko Tamara; Heimbach Veronika; Vetter Claudia S; Brocker Eva B; Rapp Ulf R
CS Institut fur Medizinische Strahlenkunde und Zellforschung (MSZ), University Clinics of Wurzburg, Versbacher Str. 5, 97078 Wurzburg, Germany.. joachim.fensterle@mail.uni-wuerzburg.de
SO BMC cancer, (2004 Sep 12) Vol. 4, pp. 62. Electronic Publication: 2004-09-12.
Journal code: 100967800. E-ISSN: 1471-2407.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200503
ED Entered STN: 28 Sep 2004
Last Updated on STN: 9 Mar 2005
Entered Medline: 8 Mar 2005
AB BACKGROUND: Mutations of the BRAF gene are the most common genetic alteration in melanoma. Moreover, BRAF mutations are already present in benign nevi. Being overexpressed and mutated, B-Raf is a potential target for the immune system and as this mutation seems to be an early event, a humoral immune response against this antigen might serve as a diagnostic tool for detection of high risk patients. METHODS: 372 sera of 148 stage IV melanoma patients and 119 sera of non-melanoma patients were screened for B-Raf, B-Raf V599E and C-Raf specific antibodies by an ELISA assay. Sera were screened for specific total Ig and for IgG. Serum titers were compared with a two tailed Mann-Whitney U test. Sera with titers of 1:300 or higher were termed positive and groups were compared with a two tailed Fisher's exact test. RESULTS: B-Raf specific antibodies recognizing both B-Raf and B-Raf V599E were detected in 8.9% of the sera of melanoma patients and in 2,5% of the control group. Raf specific IgG was detected in some patients at very low levels. B-Raf specific antibody responses did not correlate with clinical parameters but in some cases, B-Raf antibodies emerged during disease progression. CONCLUSION: These findings

imply that B-Raf is immunogenic in melanoma patients and that it might serve as a potential target for immunotherapy. However, B-Raf specific antibodies emerge at rather late stages of melanoma progression and are present only with a low frequency indicating that spontaneous B-Raf specific antibodies are not an early marker for melanoma, but rather may serve as a therapeutic target.

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
AN 2004:832664 CAPLUS
DN 141:311824
TI B-Raf specific antibody responses in melanoma patients
AU Fensterle, Joachim; Becker, Jurgen C.; Potapenko, Tamara; Heimbach, Veronika; Vetter, Claudia S.; Brocker, Eva B.; Rapp, Ulf R.
CS Institut fuer Medizinische Strahlenkunde und Zellforschung (MSZ), University Clinics of Wuerzburg, Wuerzburg, 97078, Germany
SO BMC Cancer (2004), 4, No pp. given
CODEN: BCMACL; ISSN: 1471-2407
URL: http://www.biomedcentral.com/content/pdf/1471-2407-4-62.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Background Mutations of the BRAF gene are the most common genetic alteration in melanoma. Moreover, BRAF mutations are already present in benign nevi. Being overexpressed and mutated, B-Raf is a potential target for the immune system and as this mutation seems to be an early event, a humoral immune response against this antigen might serve as a diagnostic tool for detection of high risk patients. Methods 372 sera of 148 stage IV melanoma patients and 119 sera of non-melanoma patients were screened for B-Raf, B-Raf V599E and C-Raf specific antibodies by an ELISA assay. Sera were screened for specific total Ig and for IgG. Serum titers were compared with a two tailed Mann-Whitney U test. Sera with titers of 1:300 or higher were termed pos. and groups were compared with a two tailed Fisher's exact test. Results: B-Raf specific antibodies recognizing both B-Raf and B-Raf V599E were detected in 8.9 % of the sera of melanoma patients and in 2.5 % of the control group. Raf specific IgG was detected in some patients at very low levels. B-Raf specific antibody responses did not correlate with clin. parameters but in some cases, B-Raf antibodies emerged during disease progression. Conclusion: These findings imply that B-Raf is immunogenic in melanoma patients and that it might serve as a potential target for immunotherapy. However, B-Raf specific antibodies emerge at rather late stages of melanoma progression and are present only with a low frequency indicating that spontaneous B-Raf specific antibodies are not an early marker for melanoma, but rather may serve as a therapeutic target.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 41 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:123545 BIOSIS
DN PREV200300123545
TI Recombinant intra-cellular bacteria as carriers for tumor antigens.
AU Gunn, George R. III [Reprint Author]; Zubair, Abba C.; Paterson, Yvonne
CS Department of Microbiology, University of Pennsylvania, Philadelphia, PA, 19104, USA
yvonne@mail.med.upenn.edu
SO Dietrich, Guido [Editor, Reprint Author]; Goebel, Werner [Editor]. (2002) pp. 315-348. Vaccine delivery strategies. print.
Publisher: Horizon Scientific Press, P. O. Box 1, Wymondham, Norfolk, NR18 0EH, UK.
ISBN: 1-898486-48-4 (cloth).
DT Book; (Book Chapter)
LA English
ED Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003

=> d bib ab 8

L2 ANSWER 8 OF 41 MEDLINE on STN
AN 2002632380 MEDLINE
DN PubMed ID: 12390832
TI Dendritic cells: another possible carrier for gastrointestinal bacterial translocation.
AU Lu Jing-Bo; Shi Han-Ping
CS Department of General Surgery, Nanfang Hospital, First Military Medical University, Guangzhou 510515, China.
SO Di 1 jun yi da xue xue bao = Academic journal of the first medical college of PLA, (2002 Jan) Vol. 22, No. 1, pp. 17-9.
Journal code: 9426110. ISSN: 1000-2588.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 23 Oct 2002
Last Updated on STN: 13 Dec 2002
Entered Medline: 7 Nov 2002
AB OBJECTIVE: To observe the immigration and morphological changes of peripheral dendritic cells (DCs) after hemorrhagic shock and to understand the role of DCs in bacterial translocation (BT) from the gastrointestinal tract. METHODS: Forty-eight Wistar rats were randomly divided into sham-operated group (n=8) which did not receive phlebotomy and hemorrhagic shock group (n=40) in which hemorrhagic shock was induced with Wigger's method, with the carotid pressure manipulated at 5.3 kPa for 1 h before resuscitation by transfusion of the blood from previous phlebotomy along with infusion of Ringer's solution of the same volume. Using sterile technique, the mesenteric lymph nodes (MLNs) were sampled at 3, 6, 12, 24 and 48 h respectively (n=8) following the resuscitation, and immunohistochemical study and bacterial culture were conducted. RESULTS: In the sham-operated group, bacterial culture yielded only 1 positive results, while in the hemorrhagic shock group all animals were shown positive for bacteria. The number of DCs and amount of the bacteria in the MLNs increased significantly after hemorrhagic shock, both reaching the maximum at 12 h in a highly correlative manner (r=0.89). Morphologically, DCs in the hemorrhagic shock group with abundant dendritic processes differed from those of the sham-operated rats, the latter with scarce changes during the experiment. CONCLUSION: Hemorrhagic shock results in morphological and functional transformations of gastrointestinal DCs, the number of which is in positive correlation with

the amount of bacteria in the MLN, indicating that DCs, besides the macrophages, are also important bacteria carriers during the generation of BT.

=> d bib ab 10

L2 ANSWER 10 OF 41 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 5
AN 2002:417178 BIOSIS
DN PREV200200417178
TI Bacterial carriers and virus-like-particles as antigen delivery devices: Role of dendritic cells in antigen presentation.
AU Beyer, Thomas; Herrmann, Martin; Reiser, Christian; Bertling, Wolf; Hess, Juergen [Reprint author]
CS Department of Molecular Therapy, November AG, Ulrich-Schalk-Str. 3, D-91056, Erlangen, Germany
hess@november.de
SO Current Drug Targets - Infectious Disorders, (November, 2001) Vol. 1, No. 3, pp. 287-302. print.
ISSN: 1568-0053.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 31 Jul 2002
Last Updated on STN: 31 Jul 2002